ERIN E. MURPHY, Januari NE D. MATTSON, ELIZABETH ESTHER MARY BATES. DANIEL M. GORMAN and SERGE J.E. LEBECOUE Application No.: Page 2

Please also amend the specification by deleting Sequence Submission pp. 84-110, and substitute therefore the attached Sequence Submission, pp. 84-108.

# **REMARKS**

The amendments to the related application section provide the filing dates for the individual priority applications from which this application claims benefit.

The amendments to the sequence listing correct various formalities in the originally filed listing of the parent application. No new matter is added thereby.

The Applicants also attach a request under 37 C.F.R. § 1.821(e) that the computer-readable form filed in the parent Application No. 09/351,777 be used as the computerreadable form for the instant application.

I hereby state that the informational contents of the paper and computer readable copies of the above Sequence Listing are believed to be the same. This submission involves no new matter as the enclosed sequences are the same as those filed in the priority documents.

# CONCLUSION

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

Reg. No. 46,946

TOWNSEND and TOWNSEND and CREW LLP Two Embarcadero Center, 8th Floor San Francisco, California 94111-3834

Tel: (415) 576-0200 Fax: (415) 576-0300

FJM:meg SF 1215778 v1

#### **VERSION WITH MARKINGS TO SHOW CHANGES**

# In the Specification:

This application is a Continuation Application of U.S. Patent Utility Application No. 09/351,777 filed on July 12, 1999. USSN 09/351,777 was a conversion to a U.S. Utility Patent Application of U.S. Provisional Patent Application of USSN 60/092,658 which was filed on July 13, 1998; USSN 60/093,897 which was filed on July 23, 1998; and USSN 60/099,999 which was filed on September 11, 1998. This application incorporates herein by reference, and claims priority to, each of these four applications. [This filing is a conversion to a U.S. Utility Patent Application of U.S. Provisional Patent Applications USSN 60/092,658; USSN 60/093,897; and USSN 60/099,999; each of which is incorporated herein by reference].



### SEQUENCE SUBMISSION

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        SEQ ID NO: 2 is a primate HDTEA84 amino acid sequence.
        SEQ ID NO: 3 is a primate HSLJD37R nucleic acid sequence.
        SEQ ID NO: 4 is a primate HSLJD37R amino acid sequence.
        SEQ ID NO: 5 is supplemented primate HSLJD37R nucleic acid sequence.
        SEQ ID NO: 6 is supplemented primate HSLJD37R amino acid sequence.
        SEQ ID NO: 7 is variant primate HSLJD37R nucleic acid sequence.
        SEQ ID NO: 8 is variant primate HSLJD37R amino acid sequence. SEQ ID NO: 9 is murine TNF-R2 amino acid sequence.
  10
        SEQ ID NO: 10 is human TWF-R2 amino acid sequence.
        SEQ ID NO: 11 is human OAG amino acid sequence.
        SEQ ID NO: 12 is a rodent\RANKL nucleic acid sequence.
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Ser Gln Asn Thr Gln Cys Gln Pro Cys Pro Pro Gly Thr Phe Ser Ala

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MURPHY, et al.

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94 MURRHY, et al. 85 80 75 Arg Glu Cys Thr Cys Pro Pro Gly Met Phe Gln Ser Asn Ala Thr Cys Ala Pro His Thr Val Cys Pro Val Gly Trp Gly Val Arg Lys Lys Gly 105 Thr Glu Thr Glu Asp Val Arg Cys Lys Gln Cys Ala Arg Gly Thr Phe 120 Ser Asp Val Pro\Ser Ser Val Met Lys Cys Lys Ala Tyr Thr Asp Cys Leu Ser Gln Asn Leu Val Val Ile Lys Pro Gly Thr Lys Glu Thr Asp 155 Asn Val Cys Gly Thr\Leu Pro Ser Phe Ser Ser Ser Thr Ser Pro Ser 175 Pro Gly Thr Ala Ile Phe Pro Arg Pro Glu His Met Glu Thr His Glu Val Pro Ser Ser Thr Tyr Val Pro Lys Gly Met Asn Ser Thr Glu Ser Asn Ser Ser Ala Ser Val Arg Pro Lys Val Leu Ser Ser Ile Gln Glu 225 Gly Thr Val Pro Asp Asn Thr\Ser Ser Ala Arg Gly Lys Glu Asp Val

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Asn Lys Thr Leu Pro Asn Leu Gln Val Val Asn His Gln Gln Gly Pro

35 His His Arg His Ile Leu Lys Leu Leu Pro Ser Met Glu Ala Thr Gly 270 265

Gly Glu Lys Ser Ser Thr Pro Ile Lys Gly Pro Lys Arg Gly His Pro 290 40

Arg Gln Asn Leu His Lys His Phe Asp Tle Asn Glu His Leu Pro Trp 3,05

Met Ile Val Leu Phe Leu Leu Leu Val Leu Val Val Ile Val Val Cys 45 320

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Ile Tyr Gln Phe Leu Cys Asn Ala Ser Glu Arg Glu Val Ala Ala Phe 60

95 MURPHY, et al. 405 400 395 Ser Asn Gly Tyr Thr Ala Asp His Glu Arg Ala Tyr Ala Ala Leu Gln 5 His Trp Thr Ile Arg Gly Pro Glu Ala Ser Leu Ala Gln Leu Ile Ser 430 Ala Leu Arg Gln His Arg Arg Asn Asp Val Val Glu Lys Ile Arg Gly 450 10 Leu Met Glu Ask Thr Thr Gln Leu Glu Thr Asp Lys Leu Ala Leu Pro 460 Met Ser Pro Ser Rro Leu Ser Pro Ser Pro Ile Pro Ser Pro Asn Ala 15 480 475 Lys Leu Glu Asn Sex Ala Leu Leu Thr Val Glu Pro Ser Pro Gln Asp 495 20 Lys Asn Lys Gly Phe Phe Val Asp Glu Ser Glu Pro Leu Leu Arg Cys 510 Asp Ser Thr Ser Ser Gly\Ser Ser Ala Leu Ser Arg Asn Gly Ser Phe 530 25 Ile Thr Lys Glu Lys Lys Asp\Thr Val Leu Arg Gln Val Arg Leu Asp 540 Pro Cys Asp Leu Gln Pro Ile Phe Asp Asp Met Leu His Phe Leu Asn 30 560 Pro Glu Glu Leu Arg Val Ile Glu Glu Ile Pro Gln Ala Glu Asp Lys 575 580 35 Leu Asp Arg Leu Phe Glu Ile Ile oly Val Lys Ser Gln Glu Ala Ser 590 585 Gln Thr Leu Leu Asp Ser Val Tyr Ser\His Leu Pro Asp Leu Leu 40 605 <210> 7 <211> 1474 <212> DNA 45 <213> primate <220> <221> CDS 50 <222> (1)..(1332)

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-30

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SF0818	K
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	\$	ctt (	gga Gly	ttc : Phe :	ctt Leu	agc Ser -5	acc Thr	acc Thr	aca Thr	gct Ala -1	cag Gln 1	Pro	gaa Glu	cag Gln	aag Lys 5	gcc Ala	tcg Ser	144
1	0	aat ( Asn )	ctc Leu	att Ile 10	ejy ggc	aca Thr	tac Tyr	cgc Arg	cat His 15	gtt Val	gac Asp	cgt Arg	gcc Ala	acc Thr 20	ggc Gly	cag Gln	gtg Val	192
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Thus II II IIIII	35	gcc Ala	ccc Pro 105	His	acg Thr	gtg Val	tgt Cys	ect Pro	o vas	g ggt	tgg Tr	g ggt	t gtg Y Val	. Alg	aag Lys	aaa Lys	Gly	480
the dust due		aca Thr 120	Glu	act Thr	gag Glu	gat Asp	gtg Val 125	. Arg	g tg g Cy:	t aag	g cag s Gl	n Cy	t gct s Ala 0	cgg A Arg	ggt Gly	acc Thr	ttc Phe 135	·528
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	45	ctg Leu	agt Ser	cag Glr	aac Asr 159	ı Lev	g gtg ı Val	g gt l Va	g at 1 Il	c aa e Ly 16	S PL	g gg	g ac y Th	c aaq r Lys	g gag s Glu 169		gac Asp	624
•	50	aac Asn	gto Val	tgt L Cys 170	s Gly	c aca y Thi	a cto	c cc u Pr	g to o Se 17	r Pii	c to e Se	c ag r Se	c tc r Se	c acc r Th		a cct r Pro	tcc Ser	672
	55	cct Pro	gg ( Gl)	/ Thi	a gco r Ale	c ato a Ilo	c tt e Ph	t cc e Pr 19	o Ar	gc cc g Pr	t ga o Gl	ıg ca .u Hi	ic\at is Me	_	a ac u Th	c cat r His	gaa Glu	720
		gto Va 200	c cc		c tc r Se	c ac r Th	t ta r Ty 20	r Va	t co	c aa co Ly	aa gg /s G]	TA LIE	g að et As	n Se	a ac r Th	a gaa r Gl	a tcc u Ser 215	
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draft draft	20	aga c Arg G	ag aa 31n As	c cta n Leu	cac His 300	aag Lys	cat His	ttt Phe	gac Asp	atc Ile 305	Asn	gag Glu	cat His	ttg Leu	ccc Pro 310	tgg Trp	1056
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The The same of th	30	agt a Ser l	atc cg [le Ar 33	g Lys	agc Ser	tcg Ser	agg Arg	act Thr 335	Leu	aaa Lys	aag Lys	Gly	ccc Pro 340	Arg	cag Gln	gat Asp	1152
dwy H Henry	35	Pro S	agt go Ser Al 345	c att a Ile	gtg Val	gaa Glu	aag Lys 350	Ala	ggg	ctg Leu	aag Lys	aaa Lys 355	Ser	atg Met	act Thr	cca Pro	1200
out in the man		acc of Thr (	cag aa Gln As	c cgg n Arg	g gag g Glu	aaa Lys 365	Tr	ato lle	tac Tyr	tac Tyr	tgc Cys	ASI	ggc	cat His	gga Gly	Pro 375	1248
	40	cat (	gat ga Asp Gl	ıg gaç .u Glı	g tgg ı Trp 380	Gly	tto Lev	n atg Met	gag Gļu	g aga 1 Arc 385	j nis	att Ile	caa Glr	gat Asp	att 11e 390		1296
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1b

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Glu Lys Ser Ser Thr Pro Ile Lys Gly Pro Lys Arg Gly His Pro Gly 285 280 Arg Gln Asn Leu His Lys His Phe Asp Ile Asn Glu His Leu Pro Trp 305 Met Ile Val Leu Phe Leu Leu Leu Val Leu Val Val Ile Val Val Cys Ser Ile Arg Lys Ser Ser Arg Thr Leu Lys Lys Gly Pro Arg Gln Asp Pro Ser Ala tle Val Glu Lys Ala Gly Leu Lys Lys Ser Met Thr Pro Thr Gln Asn Ard Glu Lys Trp Ile Tyr Tyr Cys Asn Gly His Gly Pro 365 His Asp Glu Glu Trp Gly Leu Met Glu Arg His Ile Gln Asp Ile Tyr Ile Gln Arg Ser Asn Gln Asp Ser Glu Arg Trp Gly <210> 9 <211> 227 <212> PRT 30 <213> rodent <400> 9 Met Ala Pro Ala Ala Leu Tro Val Ala Leu Val Phe Glu Leu Gln Leu Trp Ala Thr Gly His Thr Val Pro Ala Gln Val Val Leu Thr Pro Tyr Lys Pro Glu Pro Gly Tyr Glu Cys Gln Ile Ser Gln Glu Tyr Tyr Asp Arg Lys Ala Gln Met Cys Cys Ala Lys Cys Pro Pro Gly Gln Tyr Val Lys His Phe Cys Asn Lys Thr Ser Asp\Thr Val Cys Ala Asp Cys Glu Ala Ser Met Tyr Thr Gln Val Trp Asn Gin Phe Arg Thr Cys Leu Ser Cys Ser Ser Ser Cys Thr Thr Asp Gln Val\Glu Ile Arg Ala Cys Thr Lys Gln Gln Asn Arg Val Cys Ala Cys Glu Ala Gly Arg Tyr Cys Ala

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Cys Gly Pro Gly Phe Gly Val Ala Ser Ser Arg Ala Pro Asn Gly Asn

140

SF0818K 100 MURPHY, et al. 155 160 150 145 Val Lew Cys Lys Ala Cys Ala Pro Gly Thr Phe Ser Asp Thr Thr Ser 170 165 Ser Thr Asp Val Cys Arg Pro His Arg Ile Cys Ser Ile Leu Ala Ile Pro Gly Asn\Ala Ser Thr Asp Ala Val Cys Ala Pro Glu Ser Pro Thr 10 Leu Ser Ala Ile Pro Arg Thr Leu Tyr Val Ser Gln Pro Glu Pro Thr 215 Arg Ser Gln 225 <210> 10 210 <211> 225 <212> PRT <213> primate the design of the state of the <400> 10 Met Ala Pro Val Ala Val Trp Ala Ala Leu Ala Val Gly Leu Glu Leu 25 Trp Ala Ala Ala His Ala Lèu Pro Ala Gln Val Ala Phe Thr Pro Tyr T. I 30 -H Ala Pro Glu Pro Gly Ser Thr Cys Arg Leu Arg Glu Tyr Tyr Asp Gln £ Thr Ala Gln Met Cys Cys Ser Lys Cys Ser Pro Gly Gln His Ala Lys ſij. 35 Val Phe Cys Thr Lys Thr Ser Asp Thr Val Cys Asp Ser Cys Glu Asp C) 70 ļ,L Ser Thr Tyr Thr Gln Leu Trp Asn Trp Val Pro Glu Cys Leu Ser Cys 40 Gly Ser Arg Cys Ser Ser Asp Gln Val Glu Thr Gln Ala Cys Thr Arg 105 45 Glu Gln Asn Arg Ile Cys Thr Cys Arg Pro Gly Trp Tyr Cys Ala Leu Ser Lys Gln Glu Gly Cys Arg Leu Cys Ala Pro Leu Arg Lys Cys Arg 50 135 Pro Gly Phe Gly Val Ala Arg Pro Gly Thr Glu Thr Ser Asp Val Val Cys Lys Pro Cys Ala Pro Gly Thr Phe Ser Asn Tha Thr Ser Ser Thr 55 170 Asp Ile Cys Arg Pro His Gln Ile Cys Asn Val Val Ala Ile Pro Gly 190

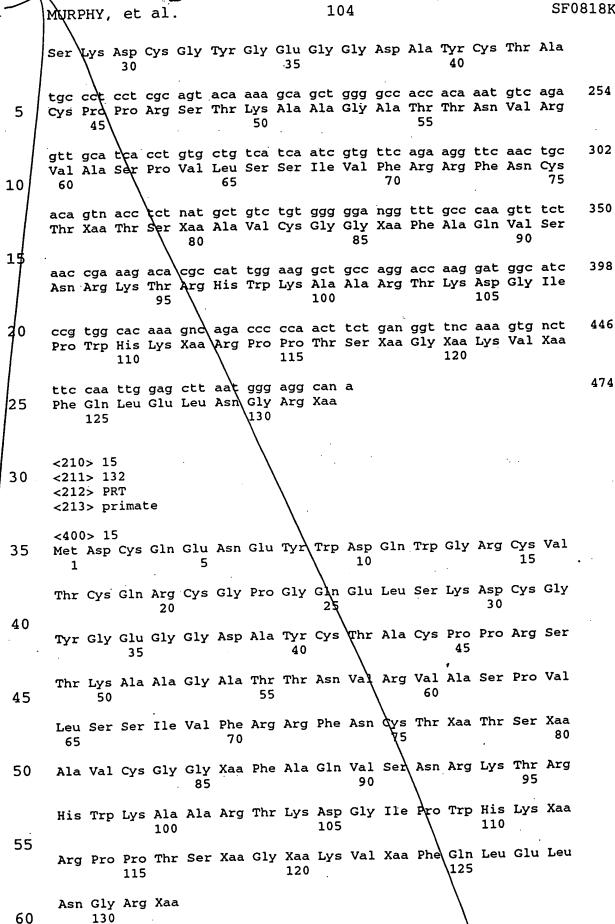
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		ctc cac ctg gca tgt aaa gtg agt tgc gaa acc gga gat tgc agg cag 211 Leu His Leu Ala Cys Lys Val Ser Cys Glu Thr Gly Asp Cys Arg Gln -5 -1 1 5
A fort	20	cag gaa ttc aag gat cga tct gga aac tgt gtc ctc tgc aaa cag tgc 259 Gln Glu Phe Lys Asp Arg Ser Gly Asn Cys Val Leu Cys Lys Gln Cys 10 20
remains of the control of the contro	25	gga cct ggc atg gag ttg tcd aag gaa tgt ggc ttc ggc tat ggg gag 307 Gly Pro Gly Met Glu Leu Ser Lys Glu Cys Gly Phe Gly Tyr Gly Glu 25 30
1	30	gat gca cag tgt gtg ccc tgc agg ccg cac cgg ttc aag gaa gac tgg 355 Asp Ala Gln Cys Val Pro Cys Arg Pro His Arg Phe Lys Glu Asp Trp 40 55
deng deng mang ng geng Hayli History Hassa H Hayli Hayli	35	ggt ttc cag aag tgt aag cca tgt gcg gac tgt gcg ctg gtg aac cgc 403 Gly Phe Gln Lys Cys Lys Pro Cys Ala Asp Cys Ala Leu Val Asn Arg 60 70
The first than	4.0	ttt cag agg gcc aac tgc tca cac acc agt gat gct gtc tgc ggg gac 451 Phe Gln Arg Ala Asn Cys Ser His Thr Ser Asp Ala Val Cys Gly Asp 75 80 85
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	5	Cyr Gly Glu Gly Asp Ala Tyr Cys Thr Ala Cys Pro Pro Arg Arg
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	25	<pre>&lt;220&gt; &lt;221&gt; misc_feature &lt;222&gt; (782) &lt;223&gt; N; may be A, C, G, or T</pre>
	30	c400> 18 cgcgctgagg tggatttgta ccggagtccc atttgggagc aagagccatc tactcgtccg 60
1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	35	ttaccggcct tcccacc atg gat tgc caa gaa aat gag tac tgg gac caa 110  Met Asp Cys Gln Glu Asn Glu Tyr Trp Asp Gln  1 5 10
TREET HOLE OF THE LAND THE TREET THE		tgg gga cgg tgt gtc acc tgc caa cgg tgt ggt cct gga cag gag cta 158  Trp Gly Arg Cys Val Thr Cys Gln Arg Cys Gly Pro Gly Gln Glu Leu  15 20 25
	40	tcc aag gat tgt ggt tat gga gag ggt gga gat gcc tac tgc aca gcc 206 Ser Lys Asp Cys Gly Tyr Gly Glu Gly Gly Asp Ala Tyr Cys Thr Ala 30 35 ,40
	45	tgc cct cct cgc agg tac aaa agc agc tgg ggc cac cac aaa tgt cag 254 Cys Pro Pro Arg Arg Tyr Lys Ser Ser Trp Gly His His Lys Cys Gln 45 50 55
į	50	agt tgc atc acc tgt gct gtc atc aat cgt gtt cag aag gtc aac tgc 302 Ser Cys Ile Thr Cys Ala Val Ile Asn Arg Val Gln Lys Val Asn Cys 60 65 70 75
	55	aca gct acc tct aat gct gtc tgt ggg gac tgt ttg\ccc agg ttc tac 350 Thr Ala Thr Ser Asn Ala Val Cys Gly Asp Cys Leu Pro Arg Phe Tyr 80 85 90
		cga aag aca cgc att gga ggc ctg cag gac caa gag tgc atc ccg tgc 398 Arg Lys Thr Arg Ile Gly Gly Leu Gln Asp Gln Glu Cys Ile Pro Cys 95 100 105
	60	·

Suh AZ MURPHY, 107 et al. acg aag cag acc ccc acc tct gag gtt caa tgt gcc ttc cag ttg agc Thr Lys Gln Thr Pro Thr Ser Glu Val Gln Cys Ala Phe Gln Leu Ser 11/0 115 tta gtg gag/gca gat gca ccc aca gtg ccc cct cag gag gcc aca ctt Leu Val Glu Ala Asp Ala Pro Thr Val Pro Pro Gln Glu Ala Thr Leu 130 125 gtt gca ctg gtg agc agc ctg cta gtg gtg ttt acc ctg gcc ttc ctg Val Ala Leu Val Ser Ser Leu Leu Val Val Phe Thr Leu Ala Phe Leu 145 140 ggg ctc ttc ttc  $\Delta$ tc tac tgc aag cag ttc ttc aac aga cat tgc cag Gly Leu Phe Phe Lau Tyr Cys Lys Gln Phe Phe Asn Arg His Cys Gln 15 160 cqt qqa qqt ttg ctg cag ttt gag gct gat aaa aca gca aag gag gaa Arg Gly Gly Leu Leu Gln Phe Glu Ala Asp Lys Thr Ala Lys Glu Glu 175 20 tet etc tte ecc gtg cea ecc age aag gag acc agt get gag tee caa Ser Leu Phe Pro Val Pro\Pro Ser Lys Glu Thr Ser Ala Glu Ser Gln the first that the the 195 190 gtc tct tgg gcc cct ggc agc ctt gcc cag ttg ttc tct ctg gac tct Val Ser Trp Ala Pro Gly Ser Leu Ala Gln Leu Phe Ser Leu Asp Ser 210 gtt cct ata cca caa cag cag cag ggg cct gaa atg tgatgtccac Val Pro Ile Pro Gln Gln Gln Gln Gly Pro Glu Met 30 225 2 angagctaat accetacaga tggggcatat\cctatcccat cccaccagag gattgattct 840 Ŋ 35 ccatttcaca aggactgatc tggagcattt cttgcttccc tgttgtagtc tggggagcca 900 W gattccacat tcatgggact accagacatg tt'

SF0818K

494

590

638

734

780

932

155

40 <210> 19 <211> 231 <212> PRT <213> primate

<400> 19 Met Asp Cys Gln Glu Asn Glu Tyr Trp Asp Gln Trp Gly Arg Cys Val

Thr Cys Gln Arg Cys Gly Pro Gly Gln Glu Leu Ser Lys Asp Cys Gly 50

Tyr Gly Glu Gly Gly Asp Ala Tyr Cys Thr Ala Cys Pro Pro Arg Arg

Tyr Lys Ser Ser Trp Gly His His Lys Cys Gln Ser Cys Ile Thr Cys 55

Ala Val Ile Asn Arg Val Gln Lys Val Asn Cys Thr Alà Thr Ser Asn

MURPHY, et al.

A]	la	Val	Cys	Gly	Asp 85	Cys	Leu	Pro	Arg	Phe 90	Tyr	Arg	Lys	Thr	Arg 95	Ile
G]	ly	Gly	Leu	Gln 100	Asp	Gln	Glu	Cys	Ile 105	Pro	Cys	Thr	Lys	Gln 110	Thr	Pro
Tì	nr	Ser	Glu 115	Val	Gln	Cys	Ala	Phe 120	Gļn	Leu	Ser	Leu	Val 125	Glu	Ala	Asp
A.	la	Pro 130	Thr	Val	Pro	Prd	Gln 135	Glu	Ala	Thr	Leu	Val 140	Ala	Leu	Val	Sei
	er 45	Leu	Leu	Val	Val	Phe 150	The	Leu	Ala	Phe	Leu 155	Gly	Leu	Phe	Phe	Le: 160
T	γr	Cys	Lys	Gln	Phe 165	Phe	Asn	Akg	His	Cys 170	Gln	Arg	Gly	Gly	Leu 175	Lei
G:	ln	Phe	Glu	Ala 180		Lys	Thr	Ala	185	Glu	Glu	Ser	Leu	Phe 190	Pro	Va:
P	ro	Pro	Ser 195	Lys	Glu	Thr	Ser	Ala 200	Glu	Ser	Gln	Val	Ser 205	Trp	Ala	Pro
G.	ly	Ser 210	Leu	Ala	Gln	Leu	Phe 215	Ser	Leu	Asp	Ser	Val 220	Pro	Ile	Pro	Gli
	1n 25	Gln	Gln	Gly	Pro	Glu 230	Met					<u> </u>				